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Theophylline Oral Solution

DEFINITION
Theophylline Oral Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of theophylline ($C_7H_8N_4O_2$).

- IDENTIFICATION**
- **A.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.
 - **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

• **PROCEDURE**

Solution A: 10 mM [ammonium acetate](#) prepared as follows. Transfer 771 mg/L of [ammonium acetate](#) to a suitable flask, and dissolve in water. Adjust with [glacial acetic acid](#) to a pH of 5.4 and dilute with water to volume. Pass through a suitable filter of 0.2-µm pore size.

Solution B: [Methanol](#)

Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	93.5	6.5
2.5	93.5	6.5
5.0	10	90
5.1	93.5	6.5
7.0	93.5	6.5

Standard solution: 0.2 mg/mL of [USP Theophylline RS](#) in water

Sample solution: Nominally 0.2 mg/mL of theophylline from Oral Solution in water. Centrifuge and use the supernatant.

Chromatographic system
(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 270 nm. For *Identification test A*, use a photodiode array detector in the range of 210–400 nm.

Column: 2.1-mm × 10-cm; 1.7-µm packing L7

Column temperature: 40 ± 2°

Flow rate: 0.4 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of the labeled amount of theophylline ($C_7H_8N_4O_2$) in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of theophylline from the *Sample solution*

r_S = peak response of theophylline from the *Standard solution*

C_S = concentration of [USP Theophylline RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of theophylline in the *Sample solution* (mg/mL)

Acceptance criteria: 95.0%–105.0%

IMPURITIES

• ORGANIC IMPURITIES

Solution A, Solution B, Mobile phase, and Chromatographic system: Proceed as directed in the Assay.

Impurity stock solution: 0.1 mg/mL each of [USP Theophylline RS](#) and [USP Theophylline Related Compound D RS](#) in water

System suitability solution: 10 µg/mL each of [USP Theophylline RS](#) and [USP Theophylline Related Compound D RS](#) from *Impurity stock solution*, and 10 µg/mL of [USP Saccharin Sodium RS](#) in water

Standard solution: 2.0 µg/mL each of [USP Theophylline RS](#) and [USP Theophylline Related Compound D RS](#) from *Impurity stock solution* in water

Sample solution: Nominally 1.0 mg/mL of theophylline from a portion of Oral Solution in water. Centrifuge and use the supernatant.

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—See [Table 2](#) for relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between theophyllidine and saccharin, *System suitability solution*

Relative standard deviation: NMT 3.0% for theophylline and theophylline related compound D peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of theophylline related compound D in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of theophylline related compound D from the *Sample solution*

r_S = peak response of theophylline related compound D from the *Standard solution*

C_S = concentration of [USP Theophylline Related Compound D RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of theophylline in the *Sample solution* (mg/mL)

Calculate the percentage of any other individual unspecified degradation product in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any other individual unspecified degradation product from the *Sample solution*

r_S = peak response of theophylline from the *Standard solution*

C_S = concentration of [USP Theophylline RS](#) in the *Standard solution* (mg/mL)

C_U = nominal concentration of theophylline in the *Sample solution* (mg/mL)

Acceptance criteria: See [Table 2](#). Disregard peaks less than 0.1%.

Table 2